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Synthesis, x-ray crystal structure and cytotoxicity of a new tetranuclear ruthenium arene complex

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[‡] X-ray structure analysis.

Keywords

Imidazolylphosphanes, Phosphane Ligands, PN Ligands, Ruthenium

Abstract

The tetranuclear ruthenium arene compound $[(cym)_4Ru_4(\mathbf{2})Cl_6]Cl_2$ (**3**) (cym = η^6-*p*-cymene, **2** = 1,2-bis(di-*N*-methylimidazol-2-ylphosphino)ethane) was prepared and characterised by one and two dimensional NMR-techniques. Its cytotoxicity against four different cell lines was determined and, with an approximate IC_{50} of >100μM **3** can be regarded as non-toxic. Its partition coefficient in *n*-octanol/water ($\log D_{7.4}$) was also determined. The structure of complex **3** as well as of the related compound $[(cym)_2Ru_2(\mathbf{4})Cl_2]Cl_2$ (**5**) (**4** = 1,2-bis(di-*N*-methylimidazol-2-ylphosphino)ethane dioxide) were determined by single crystal structure analysis. Upon oxidation in protic solvents, ligand **2** shows P–C bond cleavage reactions to yield *P,P'*-bis(*N*-methylimidazol-2-yl)ethylene diphosphinic acid (**6**).

1. Introduction

The development of new metal-based therapeutic agents is a growing field in both bioinorganic and bioorganometallic chemistry [1-3]. Within this research area, the concept of ruthenium-arene complexes of the general formula [(η^6-arene)Ru(X)(Y)(Z)] as possible anti-cancer drugs is by now well established [4-7] and has recently been reviewed [8]. The common structural motif found in these compounds is a "piano-stool" geometry of the ruthenium center, coordinated by one arene ligand as the "seat" and three other ligands that build the "legs". Therein, X and Y can be either two monodentate ligands or one bidentate chelating ligand and Z usually is a leaving group. In recent years, especially compounds like the RAPTA complexes [9-11] have emerged as water-soluble examples in this class, bearing one water-soluble phosphane ligand. Enhancing the water solubility and tuning the compounds hydrophilic/hydrophobic balance is of great interest for the use as metallo-drug, because these features might be a means to control the biodistribution and -availability of the compound. Although examples for this concept can be found in gold phosphane complexes of the water soluble bis(dipyridylphosphino)ethane ligands [12-14], little is known about ruthenium arene complexes of these ligands.

Therefore we aimed to prepare a ruthenium-arene *P,P*-chelate complex of the imidazolyl-bisphosphine 1,2-bis(di-*N*-methylimidadol-2-ylphosphino)ethane (2-dimpe^{NMe}, **2**) that was recently developed in our group as a water-soluble diphos-type ligand [15]. The aspired monocationic complex [(cym)Ru(**2**)Cl]Cl (cym = η^6-*p*-cymene) should be highly water soluble and of the described piano-stool geometry. Similar compounds, as for example the complex [(cym)Ru(dppe)Cl]Cl are known as efficient catalyst precursors for the hydrogenation of styrene in aqueous media [16].

We herein present the results of this study, being synthesis, characterisation and X-ray crystal structure of a new ruthenium compound with four *p*-cymene ruthenium moieties that are of the piano-stool geometry. The water solubility and partition coefficient (log$D_{7.4}$) of this new multi-core complex was determined, in order to assess its hydrophobic/hydrophilic behaviour. Furthermore, the cytotoxicity was tested against different normal and cancerous cell lines, since several examples can be also found for multinuclear ruthenium compounds to exhibit DNA binding or cytotoxoic effects on various cell lines [17-22].

2. Experimental section

2.1 Synthesis

The compounds 2-dimpe^{NMe} (**2**) and [(cym)Ru(en)Cl]Cl (**7**) were synthesized according to reported procedures [15,5]. All reactions were carried out in Schlenk tubes under an atmosphere of dry nitrogen using anhydrous solvents purified according to standard procedures. All chemicals were purchased from commercial sources and used as received. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker DRX 200 and Bruker DRX 500 spectrometer. The ^{1}H spectra were calibrated against the residual proton signal of the solvent as an internal reference (methanol-d_4: δ_H = 3.31 ppm; D_2O: δ_H = 4.79 ppm) while the ^{31}P{^{1}H} NMR spectra were referenced to external 85% H_3PO_4. The MALDI mass spectra were recorded on a Bruker Ultraflex MALDI-TOF mass spectrometer. The elemental composition of the compounds was determined with a Perkin Elmer Analysator 2400 at the Institut für Pharmazeutische und Medizinische Chemie, Heinrich-Heine Universität Düsseldorf.

*2.1.1 Synthesis of [(*cym*)$_4$Ru$_4$(**2**)Cl$_6$]Cl$_2$ (**3**)*

[(cym)Ru(μ-Cl)Cl]$_2$ (**1**) (0.15 g, 0.25 mmol) and 2-dimpe^{NMe} (**2**) (50 mg, 0.12 mmol) were dissolved in 50 mL of ethanol upon gentle heating. The red solution was stored for 20 hours at -18 °C before the volume was reduced to 20 mL. Addition of diethylether (80 mL) gave the product as a crude orange precipitate, which was isolated by filtration and dried in vacuo. Yield: 100 mg (50%). ^{1}H NMR (200 MHz, 296 K, methanol-d_4, see Figure 1 for atom labelling): δ = 1.33 (d, 12H, $^{3}J_{H,H}$ = 6.9 Hz, cym-iPr, n), 1.37 (d, 12H, $^{3}J_{H,H}$ = 6.9 Hz, cym-iPr, i), 1.44 (s, broad, 4H, PCH_2CH_2P, d), 1.82 (s, 6H, cym-Me, e), 1.95 (s, 6H, cym-Me, j), 2.89 (m, 2H, cym-CH, m), 2.94 (m, 2H, cym-CH, h), 3.59 (s, broad, 12H, 2-dimpe^{NMe}, c), 5.47 (d, 4H, $^{3}J_{H,H}$ = 6.1 Hz, cym, f), 5.75 (d, 4H, $^{3}J_{H,H}$ = 6.1 Hz, cym, g), 5.77 (d, 4H, $^{3}J_{H,H}$ = 6.1 Hz, cym, k), 5.89 (d, 4H, $^{3}J_{H,H}$ = 6.1 Hz, cym, l), 7.74 (2-dimpe^{NMe}, C5H, a), 7.79 (2-dimpe^{NMe}, C4H, b). ^{13}C{^{1}H} NMR (125 MHz, 296 K, methanol-d_4): δ = 17.9 (cym-Me, e), 18.2 (cym-Me, j), 21.0 (cym-iPr, n), 21.9 (cym-iPr, i), 26.0 (PCH_2CH_2P, d), 30.7 (cym-CH, h), 31.4 (cym-CH, m), 36.9 (2-dimpe^{NMe}, c), 80.7 (cym, f), 86.3 (cym, g), 88.3 (cym, k), 90.2 (cym, l), 128.7 (2-dimpe^{NMe}, C5, a), 136.1 (2-dimpe^{NMe}, C4, b). ^{31}P{^{1}H} NMR (81 MHz, 296 K, methanol-d_4) δ = 34.3 (s). MALDI-TOF-MS: *m/z* (rel. int.) = 786 $[M]^{2+}$ (100), 650 [(cym)Ru(**2**)]$^{+}$ (50). $C_{58}H_{80}N_8Cl_8P_2Ru_4 \cdot 8H_2O$ (1783.30) calcd. C 39.0, N 6.3, H 5.4; found C 38.7, H 5.2, N 6.1. Log$D_{7.4}$ = - 0.48.

*2.1.2 Synthesis of P,P'-bis(N-methylimidazol-2-yl)ethylene diphosphinic acid (**6**)*

50 mg (0.12 mmol) of **2** were dissolved in ethanol and stirred in air for one hour. H_2O_2 (30 % in H_2O) was added dropwise and the solution was stirred at room temperature for another 8 hours. A white precipitate formed, which was filtered off and dried in vacuo to yield 38 mg of a white solid. ^{1}H NMR (200 MHz, D_2O): δ = 1.93 – 1.99 (m, 4H, PCH_2CH_2P), 4.04 (s, 6H NMe), 7.51 (s, 2H, H_{im}), 7.53 (s, 2H, H_{im}). $^{13}C\{^1H\}$ NMR (125 MHz, 296 K, methanol-d_4): δ = 24.7 (m, $PCH_2)_2$, 37.0 (s, NCH_3), 121.2 (s, CH), 127.3 (s, CH). $^{31}P\{^1H\}$ NMR (81 MHz, D_2O) δ = 17.0 (s). ESI$^-$-MS *m/z* (rel. int.) = 317 (100) $[M-H]^-$. MALDI-TOF-MS: *m/z* (rel. int.) = 318 (80) $[M]^+$, 340 (100) $[(M-H)+Na]^+$, 690 (75) $[2M+3H_2O]^+$. $C_{10}H_{22}N_4O_4P_2 \cdot 3.5H_2O$ (387.31): calcd. C 31.6, H 5.8, N 14.7; found C 31.4, H 5.5, N 14.6.

2.2 Measurement of lipophilicity (logD)

The octanol–water partition coefficient of compound **3** was determined using a shake-flask method. PBS buffered bi-destillated water (100 mL, phosphate buffer, $c(PO_4^{3-})$ = 10 mM, c(NaCl) = 0.15 M, pH adjusted to 7.4 with HCl) and *n*-octanol (100 mL) were shaken together using a laboratory shaker (Perkin-Elmer), for 72 h to allow saturation of both phases. 1 mg of **3** was mixed in 1 mL of aqueous and organic phase, respectively for 10 minutes using a laboratory vortexer. The resultant emulsion was centrifuged (3000 × g, 5 min) to separate the phases. The concentrations of **3** in the organic and aqueous phases were then determined using UV absorbance spectroscopy (230 nm). LogD_{pH} was defined as the logarithm of the ratio of the concentrations of the complex in the organic and aqueous phases (log$D$ = log{[**3**$_{(org)}$]/[**3**$_{(aq)}$]}); the value reported is the mean of three separate determinations.

2.3 Cell culture

Hct116 human colon carcinoma, Huh7 human hepatoma and H4IIE rat hepatoma cells were grown in Dulbecco´s modified Eagle´s medium (DMEM, GIBCO; Germany), A2780 human ovarian carcinoma cells were grown in RPMI cell culture medium; all media contained 10 % fetal calf serum (PAA Laboratories; Austria), penicillin (100 U / mL) and streptomycin (100 µg / mL) at 5 % CO_2 and 37 °C.

2.4 Determination of cytotoxicity

The effect of the compounds on cell viability was determined using the MTT assay [16]. Cells were plated on 96-multiwell plates (H4IIE, Hct116, Huh7 cells: 15.000 / well, A2780 cells: 35.000 / well), allowed to attach for 24 h and then treated with different concentrations of the

substances for 24. After treatment medium was changed and cells were incubated for 30 min under cell culture conditions with 1 mg / mL MTT. Then the cells were lysed with 100 % dmso. The concentration of reduced MTT as a marker for cell viability was measured photometrically (560 nm) using a Wallace Victor2 1420 multilabel counter (Perkin-Elmer).

2.5 Statistical analysis:

All data were analyzed using one-way analysis of variance, followed by Bonferroni or Dunnet post hoc analysis to determine statistical significance. *P* values < 0.05 were considered statistically significant. The analysis was performed with GraphpadPrism 5.0c.

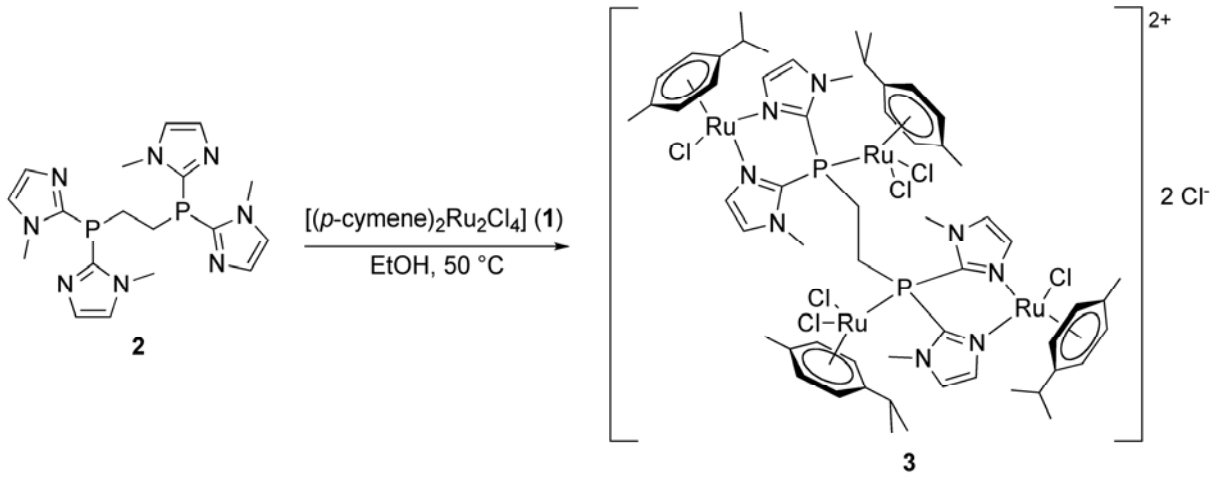
2.6 Crystallography

Crystallographic data were collected at 183(2) K on an Oxford Diffraction Xcalibur system with a Ruby detector using Mo K_α radiation (λ = 0.7107 Å) that was graphite-monochromated. Suitable crystals were covered with oil (Infineum V8512, formerly known as Paratone N), mounted on top of a glass fibre and immediately transferred to the diffractometer. The program suite CrysAlis^{Pro} was used for data collection, semi-empirical absorption correction and data reduction [23]. Structures were solved with direct methods using SIR97 [24] and were refined by full-matrix least-squares methods on F^2 with SHELXL-97 [25]. The structures were checked for higher symmetry with help of the program Platon [26]. CCDC-789984 and -789985 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

3 Results and discussion

3.1 Synthesis

Recently, we reported on the synthesis of the novel multitopic diphos-type ligand 2-dimpe^{NMe} (**2**) [15]. This ligand was designed to form complexes analogous to 1,2-bis(diphenylphosphino)ethan (dppe) complexes but shows increased hydrophilicity and water-solubility. The first attempts towards the favoured complex [(cym)Ru(**2**)Cl]Cl were carried out following a procedure described by Daguenet for [(cym)Ru(dppe)Cl]Cl [27]. However, using a metal-to-ligand ratio of 1:1 always resulted in precipitation of a light-red coloured solid which was insoluble in all common solvents and thus could not satisfyingly be characterised. Instead, other metal-to-ligand ratios were tested. Surprisingly, when [(cym)Ru(μ-Cl)Cl]$_2$ (**1**) was reacted with the ligand 2-dimpe^{NMe} (**2**) in 2 : 1 ratio, the solution stayed clear even upon cooling to -20 °C over night and the $^{31}P\{^1H\}$-NMR spectrum showed a single singlet at 34 ppm. To elucidate the composition of this new species, which was later found to be **3**, this shift was compared to the one for the chelate complex [(*p*-cymene)Ru(dppe)Cl]Cl (δ_P = 50 ppm) [16] and the bridged complex [{(*p*-cymene)RuCl$_2$}$_2$(μ-dppe)] (δ_P = 39 ppm) described by Coleman [28]. Due to the better analogy with the second complex the new species was suspected to contain *p*-cymene ruthenium moieties bridged by the diphos-ligand **2**.



2 **3**

Scheme 1. Synthesis of the four-core complex [(cym)$_4$Ru$_4$(**2**)Cl$_6$]Cl$_2$

3.2 Characterisation of **3**

Complex **3** was characterised by NMR techniques, mass spectrometry and single crystal structure determination. Full assignment of the ^{1}H NMR signals could be achieved using the two-dimensional experiments H,H- and C,H-COSY. Furthermore, NOE contacts between the imidazolyl protons and their neighbouring *p*-cymene moieties were used to unambiguously confirm the assignment (Figure 1).

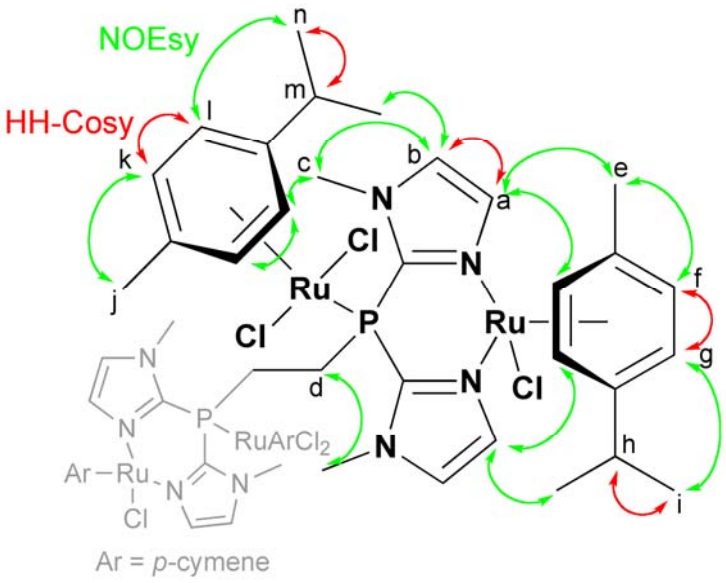


Fig. 1. Assignment of ^{1}H-NMR signals of **3** made by H,H COSY and NOESy-experiments.

The ^{1}H NMR spectrum of complex **3** (Figure 2) shows two sets of signals for the *p*-cymene protons due to two possible coordination modes of the 2-dimpe^{NMe} ligand (**2**). For each set, NOE contacts with different imidazolyl protons were found: For the cymene protons e, f, g and i NOESy cross-peaks were only observed with the imidazole-H_4 (a), whereas the imidazole-H_5 (b) gave cross-peaks with the NMe protons (c) and the isopropyl protons (n) of the second set of cymene protons (j, k, l, n) only. Furthermore, the NMe protons (c) and the aromatic protons (l) show a NOE cross signal. This specific pattern of interactions can be correlated with the rigid arrangement of the imidazolyl moieties resulting from co-ordination. Due to the restrained flexibility in the chelate ring, the NMe-groups are fixed in one position and point away from the Ru2 atoms (Figure 3). Therefore, interactions with the corresponding *p*-cymene protons are not possible.

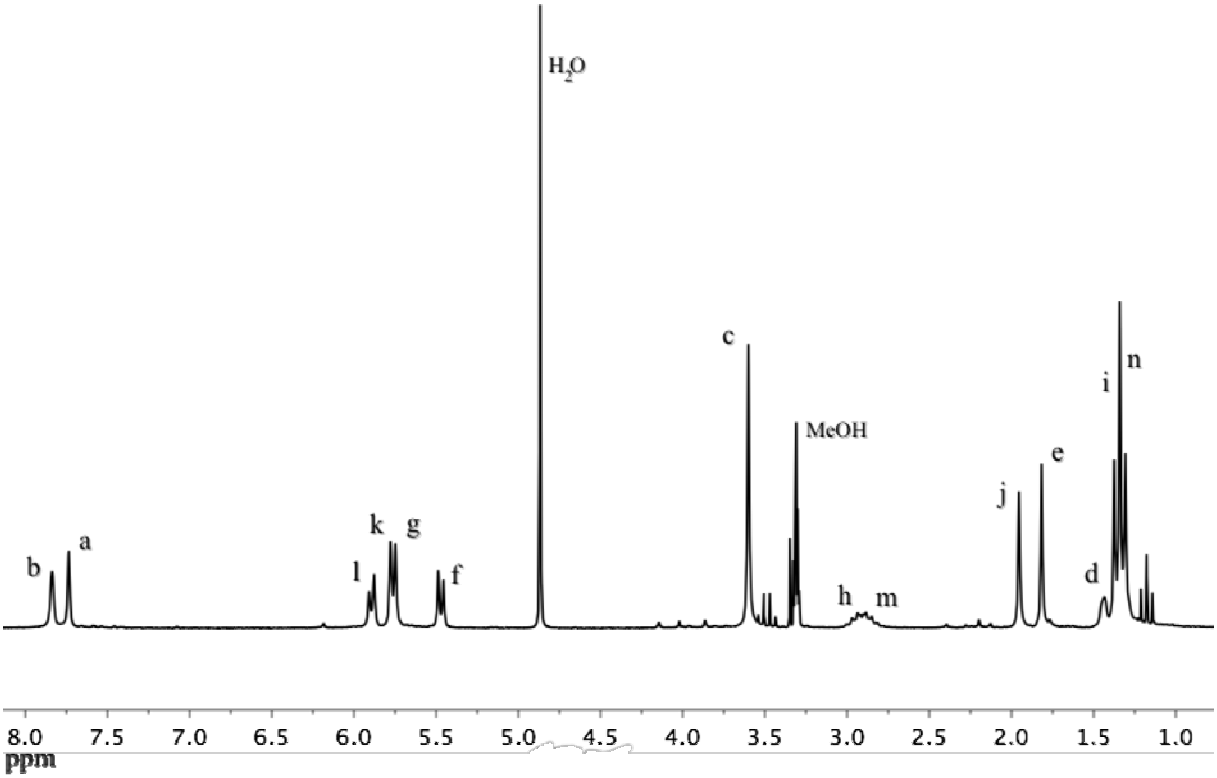
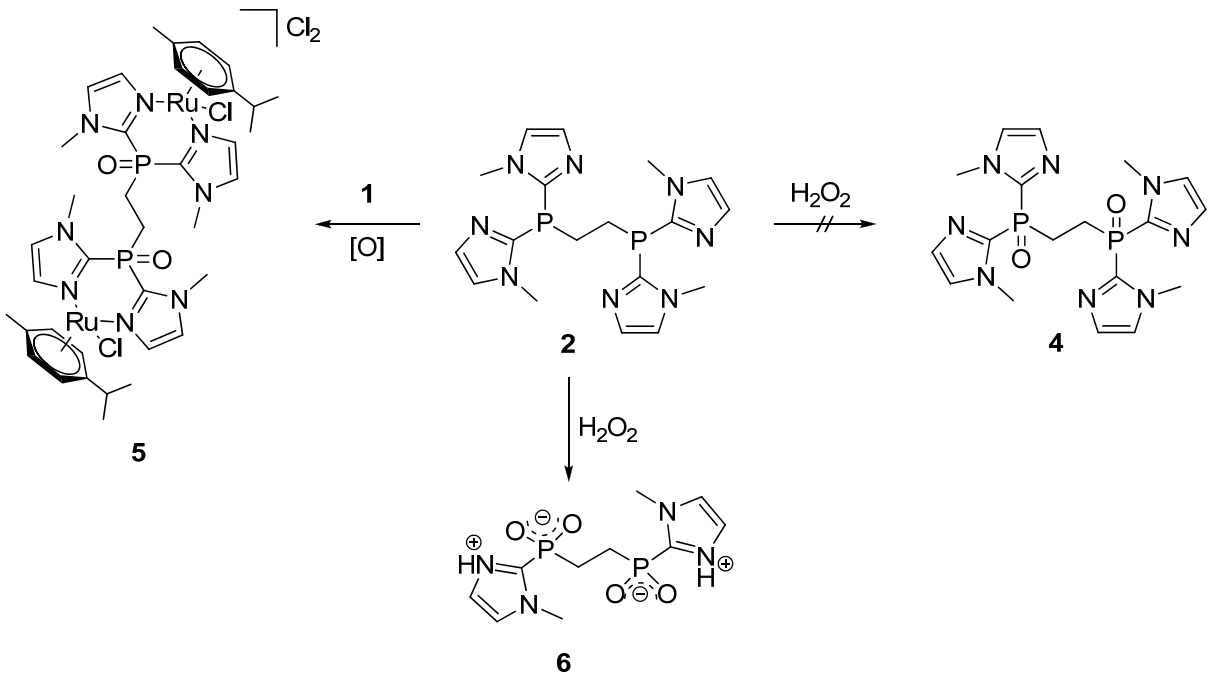


Fig. 2. ^{1}H-NMR of compound **3** with assignments derived from 2D and NOE NMR experiments.

When **3** was crystallised, additionally to the red coloured crystals of **3**, a small orange coloured crystal was found. The structure of this by-product was also analysed by single crystal analysis. It turned out, that parts of the ligand **2** oxidised during the reaction to give the dioxide **4** (Scheme 2) which can only react towards the metal with the imidazolyl-nitrogen atoms. As a result, a two-core complex [{(cym)RuCl}$_2$(μ-**4**)]Cl$_2$ (**5**) had formed in which **4** acts as a bridging bis-chelating ligand.



Scheme 2. Formation of the bridged complex [{(cym)RuCl}$_2$(μ-**4**)]Cl$_2$ (**5**) upon oxidation of the ligand **2** and decomposition of **2** to the betainic form of the phosphinic acid **6**.

3.3 Decomposition of 2-dimpe^{NMe} (**2**)

In order to establish a directed synthesis of complex **5** (Scheme 2), compound **2** was treated with different oxidising agents under various conditions. When 2-dimpe^{NMe} (**2**) was treated with H_2O_2 in methanol or ethanol, after some time, a white solid precipitated from the reaction mixture. This compound gave a single singlet in the $^{31}P\{^1H\}$-NMR spectrum at δ_P = 18 ppm, which was also found upon oxidation of **2** in methanol under air as well as upon treatment of **2** with iodosobenzene in acetonitrile. Although this ^{31}P NMR signal is shifted 74 ppm compared to free **2** in methanol (δ_P = -52 ppm) [15], the precipitate was not characterised as the dioxide **4**. One main reason for that is, that the protons of the ethylene bridge and the protons of the imidazolyl groups are found in a 4 : 4 ratio in the ^1H NMR, which suggests the loss of two imidazolyl moieties per molecule. Since furthermore, the $^{31}P\{^1H\}$-NMR shows two equivalent P atoms, the oxidation product is proposed to be *P,P'*-bis(*N*-methylimidazol-2-yl)ethylene diphosphinic acid (**6**). Additional analytical data also agree with this suggestion, whereof especially the P=O valence vibration can be used as a probe for the proposed structure. The infrared spectrum showed an intense absorption band at 1204 cm^{-1}, which was found to be the region of phosphinic acids [29]. This band is also characteristically broadened, which is thought to be a result of hydrogen bonding. Such a type of ligand decomposition by P–C cleavage reactions has already been observed in analogous monophosphanes. For example, tris(imidazol-2-yl)phosphane (2-TIP^{NH}) decomposes to the corresponding

bis(imidazol-2-yl)phosphinic acid [30, 31], and a recent example from our group also shows this reactivity for bis(*N*-methylimidazol-2-yl)phenyl phosphane (2-BIP^{NMe}) [32].

3.4 Solid state structures

Red crystals of **3**·0.8$C_4H_{10}O$ were obtained by slow diffusion of diethyl ether into a methanolic solution. Compound **3**·0.8$C_4H_{10}O$ crystallises in the monoclinic space group *C*2/c. Additionally, an orange crystal of the by-product **5**·4CH_3OH was found, which crystallises in the triclinic space group *P*-1. The crystallographic data for both structures are summarised in table 1. Tables with all angles and bond lengths can be found in the supporting information (ESI).

The coordination geometries of the ruthenium centers in **3** and **5** are best described as distorted octahedral. The metric parameters at the ruthenium atoms are within the range found in [(cym)Ru($C_4H_7N_2$)$_2$Cl]Cl [33] and [(cym)Ru(bpm)Cl]Cl (bpm = bis(pyrazolyl)methane) [34] for Ru1 of **3** and **5** and compounds [(cym)Ru(PR_3)Cl_2] for *Ru2* of **3** [35,36].

In the structures **3** and **5**, the center of the ethylene group is localized on a two-fold rotational axis and a center of inversion respectively. In both structures, the ligand **2** adopts a transoid conformation with PCCP torsion angles of 153.5(3)° and 180.0°, respectively. The substituents at the phosphorus atoms, the (cym)*Ru2*Cl_2 moieties in **3** and the O atoms in **5**, point in opposite directions. In **5**, the sterically demanding (cym)Ru1Cl substituents and the ethylene bridge adopt axial 1,4-positions, whereas in **3** both bulky (cym)Ru-moieties (at Ru1 and Ru2) are at axial positions. This steric interaction leads to the less favoured envelope conformation of the six-membered chelate rings in **3**, whereas in **5** a more boat-like conformation is found. In the structure of **3**, the cymene ligand coordinated to Ru1 is disordered in a 6:4 ratio. Essentially two rotational confirmations of the cymene could be found. In order to model this disorder, restraints had to be applied and not all non-hydrogen atoms of the disordered cymene units could be refined anisotropically.

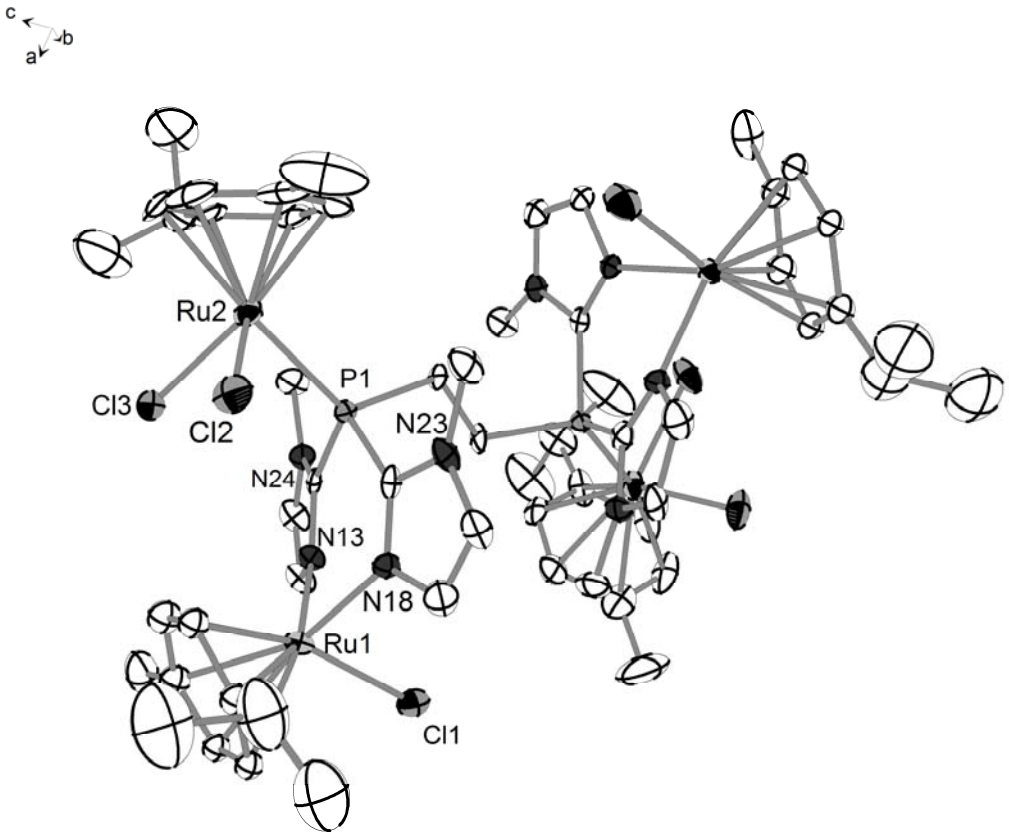


Fig. 3. Molecular structure of **3**·0.8$C_4H_{10}O$. Uncoordinated counter ions, hydrogen atoms and solvent molecules are omitted for clarity, only one conformer is shown. The displacement ellipsoids are shown on a 50 % level.

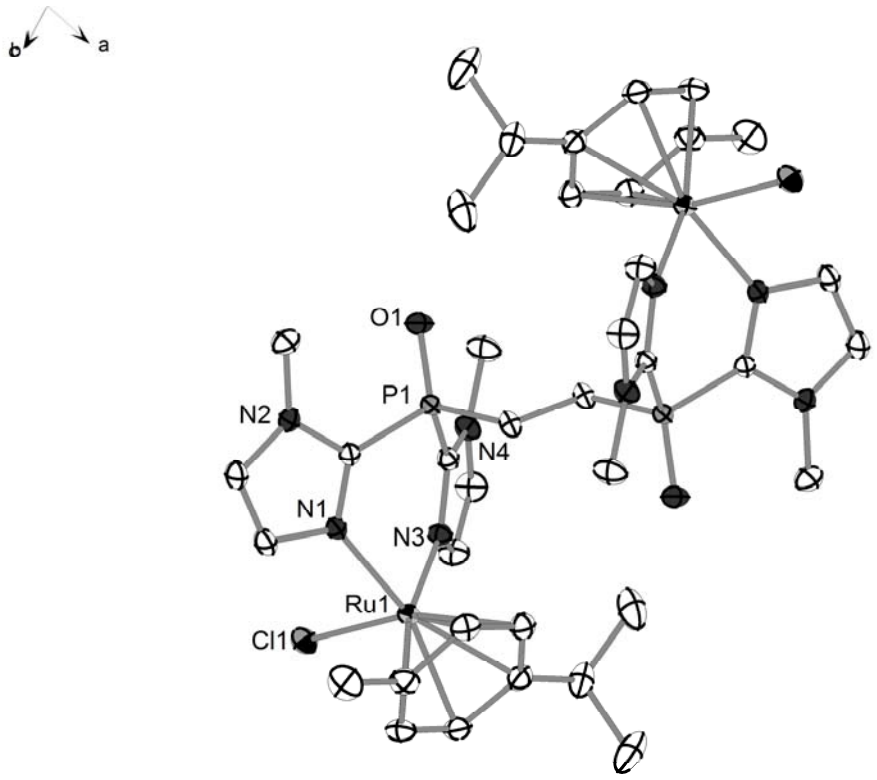


Fig. 4. Molecular structure of **5**·4CH_3OH. Uncoordinated counter ions, hydrogen atoms and solvent molecules are omitted for clarity. The displacement ellipsoids are shown on a 50 % level.

Table 1

Crystallographic data for compounds **3**·0.8$C_4H_{10}O$ and **5**·4CH_3OH.

	3·0.8$C_4H_{10}O$	**5**·4CH_3OH
Empirical formula	$C_{61.20}H_{88}Cl_8N_8O_{0.80}P_2Ru_4$	$C_{42}H_{68}Cl_4N_8O_6P_2Ru_2$
Formula weight	1698.42	1186.92
Crystal system	Monoclinic	Triclinic
Space group	*C*2/c	*P*-1
a [Å]	22.6969(7)	8.7986(1)
b [Å]	10.6605(4)	12.0206(2)
c [Å]	28.364(1)	13.7090(2)
α [°]	90	67.1764(14)
β [°]	90.334(3)	86.2548(12)
γ [°]	90	72.8348(13)
Volume [$Å^3$]	6862.9(4)	1274.88(3)
Z	4	1
Density (calculated) [Mg/m^3]	1.644	1.546
Absorption coefficient [mm^{-1}]	1.267	0.917
Crystal size [mm^3]	0.17 x 0.10 x 0.04	0.39 x 0.32 x 0.18
Crystal description	red needle	orange plate
Reflections collected	18375	58803
Independent reflections	6884 [*R*(int) = 0.0770]	12331 [*R*(int) = 0.0235]
Reflections observed	3799	11096
Completeness to theta	98.0 % to 26.37°	99.8 % to 36.32°
Max. and min. transmission	0.9511 and 0.6383	0.8523 and 0.7851
Data / restraints / parameters	6884 / 153 / 423	12331 / 0 / 312
Goodness-of-fit on F^2	0.925	1.046
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0517	*R*1 = 0.0246
	*wR*2 = 0.0896	*wR*2 = 0.0695
R indices (all data)	*R*1 = 0.1248	*R*1 = 0.0288
	*wR*2 = 0.1175	*wR*2 = 0.0708
Largest diff. peak and hole [$e.Å^{-3}$]	1.019 and -0.574	1.256 and -1.558

3.5 Solubility, distribution coefficient and cytotoxicity

Despite the four *p*-cymene ligands, compound **3** is soluble in aqueous solutions, as can be seen from a solubility of 16 g/L in water. The water-solubility is also reflected by the distribution coefficient in *n*-octanol/water of $\log D_{7.4} = -0.48$.

The cytotoxicity of compound **3** was determined in four different cell-lines using the MTT assay method. For comparison, the compound [(cym)Ru(en)Cl]Cl (**7**) (en = 1,2-diamminoethane) was also introduced in the cell line studies [5]. Cell lines used were Hct116 human colon carcinoma, Huh7 human hepatoma, H4IIE rat hepatoma and A2780 human ovarian carcinoma cells (cisplatin sensitive). As can be seen from Figure 5, compound **3** is less toxic than the reference drug **7** in various cell lines tested (H4IIE, Hct116, Huh7 and A2780 cells).

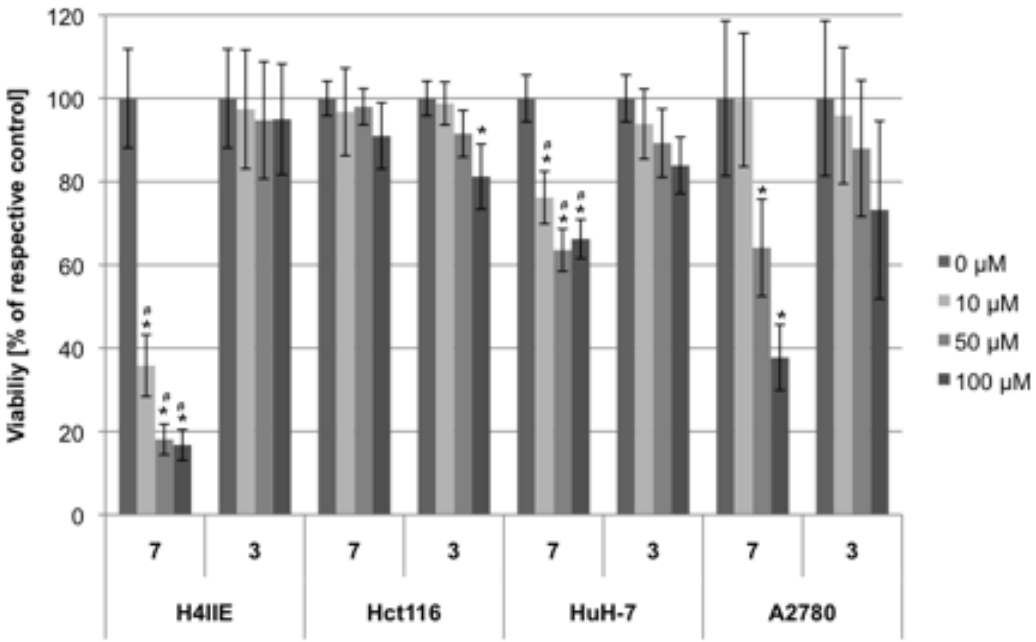


Fig. 5. Cytotoxic effects of **3** and **7** at Hct116, Huh7, H4IIE and A2780 cells. Cells were treated with different concentrations of the substances for 24. After treatment cell viability was analysed using MTT assay. The concentration of reduced MTT as a marker for cell viability was measured photometrically. Values are means +/- standard deviation, n = 3, *: $p < 0.05$ vs. control value, #: $p < 0.05$ vs. corresponding concentration of the other substance (**3** vs. **7**).

Although the IC_{50} values for the tested compounds have not been determined for all cell lines in this test, the specific value for compound **3** is greater than 100µM which is simply concluded by the observed non-toxicity up to this value. For the cell lines H4IIE and Hct116 the IC_{50} values have been determined to 705 and 393 µM, respectively. In comparison with other tetranuclear ruthenium-arene compounds, this value is particularly high. For example, rectangular shaped structures with bridging N- and O,O-ligands exhibit IC_{50} values between 4 µM and 66 µM, whereof the lowest value lies in one range with cisplatin [20]. Equally high cytotoxicities are reached with hexanuclear ruthenium assemblies which can also function as hosts for smaller drug molecules [21]. Tetranuclear ruthenium compounds with dendritic structures that seem more similar to compound **3** show IC_{50} values of 40 µM which can still be regarded as active [19,22]. With an overall charge of 2+ complex **3** ranges between the charge-neutral dendrimers and the 4+ rectangular systems but its activity might still be limited by the possibilities to pass the cell membrane.

4 Conclusion

The new tetranuclear ruthenium arene complex **3** is readily available from the common precursor $[(cym)Ru(\mu\text{-}Cl)Cl]_2$ and the water-soluble multitopic diphos-type ligand 1,2-bis(di-*N*-methylimidadol-2-ylphosphino)ethane (2-dimpe^{NMe}, **2**). In this compound, **2** unfurls truly multitopic qualities, as all six coordination sites, including the imidazolyl nitrogen atoms, are occupied by ruthenium. Interestingly, even though the nitrogen atoms are blocked, complex **3** is still quite soluble in aqueous media. Its cytotoxic activity is, however, much lower than that of known tetranuclear compounds of the ruthenium arene family. Conclusively, **3** is particularly stable in aqueous solution. In contrast to this stability, the free ligand 2-dimpe^{NMe} (**2**) undergoes P–C bond cleavage in protic solvents within a few hours. The loss of imidazolyl substituents is therein excellerated by addition of oxidising agents.

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Electronic supporting information for

Synthesis, x-ray crystal structure and cytotoxicity of a tetranuclear ruthenium arene complex

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[‡] X-ray structure analysis.

Table ESI1. Bond lengths [Å] and angles [°] for **3**·0.8$C_4H_{10}O$.

Ru(1)-N(13)	2.072(5)	C(6)-N(18)	1.323(8)
Ru(1)-N(18)	2.085(5)	C(6)-N(23)	1.358(8)
Ru(1)-C(15)	2.147(13)	C(6)-P(1)	1.824(7)
Ru(1)-C(32)	2.153(19)	C(7)-C(8)	1.338(9)
Ru(1)-C(33)	2.158(17)	C(7)-N(18)	1.383(9)
Ru(1)-C(35)	2.168(18)	C(7)-H(7A)	0.9500
Ru(1)-C(34)	2.18(2)	C(8)-N(23)	1.374(9)
Ru(1)-C(12)	2.190(14)	C(8)-H(8A)	0.9500
Ru(1)-C(13)	2.192(14)	C(9)-N(23)	1.451(8)
Ru(1)-C(14)	2.200(13)	C(9)-H(9C)	0.9800
Ru(1)-C(36)	2.201(18)	C(9)-H(9B)	0.9800
Ru(1)-C(31)	2.210(18)	C(9)-H(9A)	0.9800
Ru(2)-C(24)	2.195(7)	C(10)-C(11)	1.551(19)
Ru(2)-C(22)	2.199(7)	C(10)-H(10C)	0.9800
Ru(2)-C(23)	2.218(8)	C(10)-H(10B)	0.9800
Ru(2)-C(25)	2.225(8)	C(10)-H(10A)	0.9800
Ru(2)-C(21)	2.231(8)	C(11)-C(12)	1.33(2)
Ru(2)-C(26)	2.272(8)	C(11)-C(13)	1.373(18)
Ru(2)-P(1)	2.3407(19)	C(12)-C(14)	1.45(2)
Ru(2)-Cl(3)	2.3822(19)	C(12)-H(12A)	0.9500
Ru(2)-Cl(2)	2.401(2)	C(13)-C(15)	1.379(19)
C(1)-C(1)#1	1.531(12)	C(13)-H(13A)	0.9500
C(1)-P(1)	1.858(5)	C(14)-C(16)	1.443(18)
C(1)-H(1A)	0.9900	C(14)-H(14A)	0.9500
C(1)-H(1B)	0.9900	C(15)-C(16)	1.41(2)
C(2)-N(13)	1.321(8)	C(15)-H(15A)	0.9500
C(2)-N(24)	1.361(8)	C(16)-C(17)	1.50(2)
C(2)-P(1)	1.821(7)	C(17)-C(18)	1.41(3)
C(3)-C(4)	1.357(10)	C(17)-C(19)	1.62(2)
C(3)-N(13)	1.365(8)	C(17)-H(17)	1.0000
C(3)-H(3A)	0.9500	C(18)-H(18A)	0.9800
C(4)-N(24)	1.361(8)	C(18)-H(18B)	0.9800
C(4)-H(4A)	0.9500	C(18)-H(18C)	0.9800
C(5)-N(24)	1.460(8)	C(19)-H(19A)	0.9800
C(5)-H(5C)	0.9800	C(19)-H(19B)	0.9800
C(5)-H(5B)	0.9800	C(19)-H(19C)	0.9800
C(5)-H(5A)	0.9800	C(30)-C(31)	1.53(3)

C(30)-H(30A)	0.9800	C(43)-C(44)	1.527(10)
C(30)-H(30B)	0.9800	C(43)-H(43A)	0.9900
C(30)-H(30C)	0.9800	C(43)-H(43B)	0.9900
C(31)-C(32)	1.44(3)	C(44)-H(44A)	0.9800
C(31)-C(33)	1.51(2)	C(44)-H(44B)	0.9800
C(32)-C(34)	1.36(3)	C(44)-H(44C)	0.9800
C(32)-H(32A)	0.9500	C(20)-C(21)	1.520(12)
C(33)-C(35)	1.43(2)	C(20)-H(20A)	0.9800
C(33)-H(33A)	0.9500	C(20)-H(20B)	0.9800
C(34)-C(36)	1.38(3)	C(20)-H(20C)	0.9800
C(34)-H(34A)	0.9500	C(21)-C(22)	1.382(11)
C(35)-C(36)	1.43(3)	C(21)-C(23)	1.398(12)
C(35)-H(35A)	0.9500	C(22)-C(24)	1.418(10)
C(36)-C(37)	1.48(3)	C(22)-H(22A)	0.9500
C(37)-C(38)	1.50(3)	C(23)-C(25)	1.345(12)
C(37)-C(39)	1.531(9)	C(23)-H(23A)	0.9500
C(37)-H(37)	1.0000	C(24)-C(26)	1.400(10)
C(38)-H(38A)	0.9800	C(24)-H(24A)	0.9500
C(38)-H(38B)	0.9800	C(25)-C(26)	1.453(11)
C(38)-H(38C)	0.9800	C(25)-H(25A)	0.9500
C(39)-H(39C)	0.9800	C(26)-C(27)	1.490(11)
C(39)-H(39B)	0.9800	C(27)-C(28)	1.522(11)
C(39)-H(39A)	0.9800	C(27)-C(29)	1.540(11)
O(41)-C(43)	1.36(3)	C(27)-H(27)	1.0000
O(41)-C(42)	1.47(3)	C(28)-H(28A)	0.9800
C(41)-C(42)	1.46(3)	C(28)-H(28B)	0.9800
C(41)-H(41A)	0.9800	C(28)-H(28C)	0.9800
C(41)-H(41B)	0.9800	C(29)-H(29A)	0.9800
C(41)-H(41C)	0.9800	C(29)-H(29B)	0.9800
C(42)-H(42A)	0.9900	C(29)-H(29C)	0.9800
C(42)-H(42B)	0.9900		

N(13)-Ru(1)-N(18)	83.5(2)	C(32)-Ru(1)-C(14)	14.7(6)
N(13)-Ru(1)-C(15)	115.2(5)	C(33)-Ru(1)-C(14)	58.3(6)
N(18)-Ru(1)-C(15)	94.6(4)	C(35)-Ru(1)-C(14)	76.7(6)
N(13)-Ru(1)-C(32)	141.0(6)	C(34)-Ru(1)-C(14)	47.5(7)
N(18)-Ru(1)-C(32)	134.6(6)	C(12)-Ru(1)-C(14)	38.7(5)
C(15)-Ru(1)-C(32)	76.0(7)	C(13)-Ru(1)-C(14)	78.8(5)
N(13)-Ru(1)-C(33)	132.2(6)	N(13)-Ru(1)-C(36)	90.4(5)
N(18)-Ru(1)-C(33)	84.7(4)	N(18)-Ru(1)-C(36)	138.3(7)
C(15)-Ru(1)-C(33)	21.1(4)	C(15)-Ru(1)-C(36)	51.4(6)
C(32)-Ru(1)-C(33)	70.7(7)	C(32)-Ru(1)-C(36)	67.0(8)
N(13)-Ru(1)-C(35)	100.2(6)	C(33)-Ru(1)-C(36)	69.2(7)
N(18)-Ru(1)-C(35)	102.5(6)	C(35)-Ru(1)-C(36)	38.1(7)
C(15)-Ru(1)-C(35)	17.5(5)	C(34)-Ru(1)-C(36)	36.7(7)
C(32)-Ru(1)-C(35)	81.7(7)	C(12)-Ru(1)-C(36)	48.3(6)
C(33)-Ru(1)-C(35)	38.7(6)	C(13)-Ru(1)-C(36)	18.8(5)
N(13)-Ru(1)-C(34)	107.9(6)	C(14)-Ru(1)-C(36)	71.7(6)
N(18)-Ru(1)-C(34)	165.9(7)	N(13)-Ru(1)-C(31)	170.8(5)
C(15)-Ru(1)-C(34)	73.3(7)	N(18)-Ru(1)-C(31)	99.6(5)
C(32)-Ru(1)-C(34)	36.5(8)	C(15)-Ru(1)-C(31)	56.0(6)
C(33)-Ru(1)-C(34)	81.4(8)	C(32)-Ru(1)-C(31)	38.5(7)
C(35)-Ru(1)-C(34)	67.9(8)	C(33)-Ru(1)-C(31)	40.3(6)
N(13)-Ru(1)-C(12)	116.2(5)	C(35)-Ru(1)-C(31)	70.6(7)
N(18)-Ru(1)-C(12)	160.2(5)	C(34)-Ru(1)-C(31)	67.9(8)
C(15)-Ru(1)-C(12)	78.4(5)	C(12)-Ru(1)-C(31)	61.1(6)
C(32)-Ru(1)-C(12)	25.8(5)	C(13)-Ru(1)-C(31)	81.1(6)
C(33)-Ru(1)-C(12)	82.4(6)	C(14)-Ru(1)-C(31)	23.8(5)
C(35)-Ru(1)-C(12)	76.2(6)	C(36)-Ru(1)-C(31)	81.5(7)
C(34)-Ru(1)-C(12)	12.2(7)	C(24)-Ru(2)-C(22)	37.7(3)
N(13)-Ru(1)-C(13)	89.8(4)	C(24)-Ru(2)-C(23)	78.0(3)
N(18)-Ru(1)-C(13)	119.6(5)	C(22)-Ru(2)-C(23)	65.4(3)
C(15)-Ru(1)-C(13)	37.0(5)	C(24)-Ru(2)-C(25)	66.2(3)
C(32)-Ru(1)-C(13)	78.4(7)	C(22)-Ru(2)-C(25)	77.3(3)
C(33)-Ru(1)-C(13)	57.4(6)	C(23)-Ru(2)-C(25)	35.2(3)
C(35)-Ru(1)-C(13)	20.9(5)	C(24)-Ru(2)-C(21)	66.8(3)
C(34)-Ru(1)-C(13)	53.9(7)	C(22)-Ru(2)-C(21)	36.3(3)
C(12)-Ru(1)-C(13)	64.6(5)	C(23)-Ru(2)-C(21)	36.6(3)
N(13)-Ru(1)-C(14)	154.9(4)	C(25)-Ru(2)-C(21)	65.1(3)
N(18)-Ru(1)-C(14)	121.6(4)	C(24)-Ru(2)-C(26)	36.5(2)
C(15)-Ru(1)-C(14)	67.3(5)	C(22)-Ru(2)-C(26)	66.5(3)

C(23)-Ru(2)-C(26)	66.1(3)	N(24)-C(5)-H(5C)	109.5
C(25)-Ru(2)-C(26)	37.7(3)	N(24)-C(5)-H(5B)	109.5
C(21)-Ru(2)-C(26)	78.6(3)	H(5C)-C(5)-H(5B)	109.5
C(24)-Ru(2)-P(1)	97.62(19)	N(24)-C(5)-H(5A)	109.5
C(22)-Ru(2)-P(1)	98.1(2)	H(5C)-C(5)-H(5A)	109.5
C(23)-Ru(2)-P(1)	158.5(3)	H(5B)-C(5)-H(5A)	109.5
C(25)-Ru(2)-P(1)	159.2(3)	N(18)-C(6)-N(23)	110.0(6)
C(21)-Ru(2)-P(1)	122.3(2)	N(18)-C(6)-P(1)	128.0(5)
C(26)-Ru(2)-P(1)	121.8(2)	N(23)-C(6)-P(1)	121.8(5)
C(24)-Ru(2)-Cl(3)	118.9(2)	C(8)-C(7)-N(18)	109.1(7)
C(22)-Ru(2)-Cl(3)	156.5(2)	C(8)-C(7)-H(7A)	125.4
C(23)-Ru(2)-Cl(3)	116.0(3)	N(18)-C(7)-H(7A)	125.4
C(25)-Ru(2)-Cl(3)	91.8(2)	C(7)-C(8)-N(23)	107.1(6)
C(21)-Ru(2)-Cl(3)	152.5(2)	C(7)-C(8)-H(8A)	126.4
C(26)-Ru(2)-Cl(3)	92.1(2)	N(23)-C(8)-H(8A)	126.4
P(1)-Ru(2)-Cl(3)	84.64(6)	N(23)-C(9)-H(9C)	109.5
C(24)-Ru(2)-Cl(2)	154.3(2)	N(23)-C(9)-H(9B)	109.5
C(22)-Ru(2)-Cl(2)	116.7(2)	H(9C)-C(9)-H(9B)	109.5
C(23)-Ru(2)-Cl(2)	89.6(2)	N(23)-C(9)-H(9A)	109.5
C(25)-Ru(2)-Cl(2)	114.6(2)	H(9C)-C(9)-H(9A)	109.5
C(21)-Ru(2)-Cl(2)	89.8(2)	H(9B)-C(9)-H(9A)	109.5
C(26)-Ru(2)-Cl(2)	152.3(2)	C(11)-C(10)-H(10C)	109.5
P(1)-Ru(2)-Cl(2)	85.71(7)	C(11)-C(10)-H(10B)	109.5
Cl(3)-Ru(2)-Cl(2)	86.71(7)	H(10C)-C(10)-H(10B)	109.5
C(1)#1-C(1)-P(1)	114.3(5)	C(11)-C(10)-H(10A)	109.5
C(1)#1-C(1)-H(1A)	108.7	H(10C)-C(10)-H(10A)	109.5
P(1)-C(1)-H(1A)	108.7	H(10B)-C(10)-H(10A)	109.5
C(1)#1-C(1)-H(1B)	108.7	C(12)-C(11)-C(13)	119.8(13)
P(1)-C(1)-H(1B)	108.7	C(12)-C(11)-C(10)	119.3(16)
H(1A)-C(1)-H(1B)	107.6	C(13)-C(11)-C(10)	120.9(16)
N(13)-C(2)-N(24)	109.2(6)	C(12)-C(11)-Ru(1)	70.0(8)
N(13)-C(2)-P(1)	129.0(5)	C(13)-C(11)-Ru(1)	69.6(7)
N(24)-C(2)-P(1)	121.1(5)	C(10)-C(11)-Ru(1)	132.5(9)
C(4)-C(3)-N(13)	109.0(6)	C(11)-C(12)-C(14)	122.0(13)
C(4)-C(3)-H(3A)	125.5	C(11)-C(12)-Ru(1)	75.2(8)
N(13)-C(3)-H(3A)	125.5	C(14)-C(12)-Ru(1)	71.0(7)
C(3)-C(4)-N(24)	106.4(7)	C(11)-C(12)-H(12A)	119.0
C(3)-C(4)-H(4A)	126.8	C(14)-C(12)-H(12A)	119.0
N(24)-C(4)-H(4A)	126.8	Ru(1)-C(12)-H(12A)	126.8

C(11)-C(13)-C(15)	120.7(13)	C(17)-C(19)-H(19C)	109.5
C(11)-C(13)-Ru(1)	74.5(8)	H(19A)-C(19)-H(19C)	109.5
C(15)-C(13)-Ru(1)	69.7(8)	H(19B)-C(19)-H(19C)	109.5
C(11)-C(13)-H(13A)	119.6	C(31)-C(30)-H(30A)	109.5
C(15)-C(13)-H(13A)	119.6	C(31)-C(30)-H(30B)	109.5
Ru(1)-C(13)-H(13A)	128.4	H(30A)-C(30)-H(30B)	109.5
C(16)-C(14)-C(12)	118.4(13)	C(31)-C(30)-H(30C)	109.5
C(16)-C(14)-Ru(1)	72.2(7)	H(30A)-C(30)-H(30C)	109.5
C(12)-C(14)-Ru(1)	70.3(7)	H(30B)-C(30)-H(30C)	109.5
C(16)-C(14)-H(14A)	120.8	C(32)-C(31)-C(33)	115.6(16)
C(12)-C(14)-H(14A)	120.8	C(32)-C(31)-C(30)	125(2)
Ru(1)-C(14)-H(14A)	128.8	C(33)-C(31)-C(30)	119.1(19)
C(13)-C(15)-C(16)	123.2(14)	C(32)-C(31)-Ru(1)	68.6(10)
C(13)-C(15)-Ru(1)	73.2(8)	C(33)-C(31)-Ru(1)	68.0(9)
C(16)-C(15)-Ru(1)	74.6(8)	C(30)-C(31)-Ru(1)	134.5(15)
C(13)-C(15)-H(15A)	118.4	C(34)-C(32)-C(31)	122.6(19)
C(16)-C(15)-H(15A)	118.4	C(34)-C(32)-Ru(1)	73.0(12)
Ru(1)-C(15)-H(15A)	125.6	C(31)-C(32)-Ru(1)	72.9(10)
C(15)-C(16)-C(14)	115.6(13)	C(34)-C(32)-H(32A)	118.7
C(15)-C(16)-C(17)	122.3(16)	C(31)-C(32)-H(32A)	118.7
C(14)-C(16)-C(17)	122.0(15)	Ru(1)-C(32)-H(32A)	127.6
C(15)-C(16)-Ru(1)	68.0(7)	C(35)-C(33)-C(31)	119.1(15)
C(14)-C(16)-Ru(1)	69.8(7)	C(35)-C(33)-Ru(1)	71.1(9)
C(17)-C(16)-Ru(1)	134.6(9)	C(31)-C(33)-Ru(1)	71.7(9)
C(18)-C(17)-C(16)	112.7(17)	C(35)-C(33)-H(33A)	120.5
C(18)-C(17)-C(19)	111.5(17)	C(31)-C(33)-H(33A)	120.5
C(16)-C(17)-C(19)	107.7(13)	Ru(1)-C(33)-H(33A)	129.0
C(18)-C(17)-H(17)	108.3	C(32)-C(34)-C(36)	123(2)
C(16)-C(17)-H(17)	108.3	C(32)-C(34)-Ru(1)	70.5(11)
C(19)-C(17)-H(17)	108.3	C(36)-C(34)-Ru(1)	72.3(11)
C(17)-C(18)-H(18A)	109.5	C(32)-C(34)-H(34A)	118.7
C(17)-C(18)-H(18B)	109.5	C(36)-C(34)-H(34A)	118.7
H(18A)-C(18)-H(18B)	109.5	Ru(1)-C(34)-H(34A)	131.7
C(17)-C(18)-H(18C)	109.5	C(36)-C(35)-C(33)	120.1(16)
H(18A)-C(18)-H(18C)	109.5	C(36)-C(35)-Ru(1)	72.2(10)
H(18B)-C(18)-H(18C)	109.5	C(33)-C(35)-Ru(1)	70.3(9)
C(17)-C(19)-H(19A)	109.5	C(36)-C(35)-H(35A)	120.0
C(17)-C(19)-H(19B)	109.5	C(33)-C(35)-H(35A)	120.0
H(19A)-C(19)-H(19B)	109.5	Ru(1)-C(35)-H(35A)	130.1

C(34)-C(36)-C(35)	119.9(18)	C(44)-C(43)-H(43A)	109.7
C(34)-C(36)-C(37)	121(2)	O(41)-C(43)-H(43B)	109.7
C(35)-C(36)-C(37)	119(2)	C(44)-C(43)-H(43B)	109.7
C(34)-C(36)-Ru(1)	71.0(11)	H(43A)-C(43)-H(43B)	108.2
C(35)-C(36)-Ru(1)	69.7(10)	C(43)-C(44)-H(44A)	109.5
C(37)-C(36)-Ru(1)	130.7(12)	C(43)-C(44)-H(44B)	109.5
C(36)-C(37)-C(38)	116.7(18)	H(44A)-C(44)-H(44B)	109.5
C(36)-C(37)-C(39)	107.5(15)	C(43)-C(44)-H(44C)	109.5
C(38)-C(37)-C(39)	110.0(15)	H(44A)-C(44)-H(44C)	109.5
C(36)-C(37)-H(37)	107.4	H(44B)-C(44)-H(44C)	109.5
C(38)-C(37)-H(37)	107.4	C(21)-C(20)-H(20A)	109.5
C(39)-C(37)-H(37)	107.4	C(21)-C(20)-H(20B)	109.5
C(37)-C(38)-H(38A)	109.5	H(20A)-C(20)-H(20B)	109.5
C(37)-C(38)-H(38B)	109.5	C(21)-C(20)-H(20C)	109.5
H(38A)-C(38)-H(38B)	109.5	H(20A)-C(20)-H(20C)	109.5
C(37)-C(38)-H(38C)	109.5	H(20B)-C(20)-H(20C)	109.5
H(38A)-C(38)-H(38C)	109.5	C(22)-C(21)-C(23)	118.4(9)
H(38B)-C(38)-H(38C)	109.5	C(22)-C(21)-C(20)	123.0(9)
C(37)-C(39)-H(39C)	109.5	C(23)-C(21)-C(20)	118.6(9)
C(37)-C(39)-H(39B)	109.5	C(22)-C(21)-Ru(2)	70.6(4)
H(39C)-C(39)-H(39B)	109.5	C(23)-C(21)-Ru(2)	71.2(5)
C(37)-C(39)-H(39A)	109.5	C(20)-C(21)-Ru(2)	131.1(6)
H(39C)-C(39)-H(39A)	109.5	C(21)-C(22)-C(24)	121.0(8)
H(39B)-C(39)-H(39A)	109.5	C(21)-C(22)-Ru(2)	73.1(4)
C(43)-O(41)-C(42)	113.1(19)	C(24)-C(22)-Ru(2)	71.0(4)
C(42)-C(41)-H(41A)	109.5	C(21)-C(22)-H(22A)	119.5
C(42)-C(41)-H(41B)	109.5	C(24)-C(22)-H(22A)	119.5
H(41A)-C(41)-H(41B)	109.5	Ru(2)-C(22)-H(22A)	128.7
C(42)-C(41)-H(41C)	109.5	C(25)-C(23)-C(21)	121.7(8)
H(41A)-C(41)-H(41C)	109.5	C(25)-C(23)-Ru(2)	72.7(5)
H(41B)-C(41)-H(41C)	109.5	C(21)-C(23)-Ru(2)	72.2(5)
C(41)-C(42)-O(41)	108.6(19)	C(25)-C(23)-H(23A)	119.1
C(41)-C(42)-H(42A)	110.0	C(21)-C(23)-H(23A)	119.1
O(41)-C(42)-H(42A)	110.0	Ru(2)-C(23)-H(23A)	128.3
C(41)-C(42)-H(42B)	110.0	C(26)-C(24)-C(22)	121.0(7)
O(41)-C(42)-H(42B)	110.0	C(26)-C(24)-Ru(2)	74.7(4)
H(42A)-C(42)-H(42B)	108.4	C(22)-C(24)-Ru(2)	71.3(4)
O(41)-C(43)-C(44)	110(2)	C(26)-C(24)-H(24A)	119.5
O(41)-C(43)-H(43A)	109.7	C(22)-C(24)-H(24A)	119.5

Ru(2)-C(24)-H(24A)	126.3	C(27)-C(29)-H(29A)	109.5
C(23)-C(25)-C(26)	122.1(8)	C(27)-C(29)-H(29B)	109.5
C(23)-C(25)-Ru(2)	72.1(5)	H(29A)-C(29)-H(29B)	109.5
C(26)-C(25)-Ru(2)	72.9(4)	C(27)-C(29)-H(29C)	109.5
C(23)-C(25)-H(25A)	119.0	H(29A)-C(29)-H(29C)	109.5
C(26)-C(25)-H(25A)	119.0	H(29B)-C(29)-H(29C)	109.5
Ru(2)-C(25)-H(25A)	128.4	C(2)-N(13)-C(3)	107.3(6)
C(24)-C(26)-C(25)	115.7(8)	C(2)-N(13)-Ru(1)	130.0(5)
C(24)-C(26)-C(27)	119.0(7)	C(3)-N(13)-Ru(1)	121.3(4)
C(25)-C(26)-C(27)	125.0(7)	C(6)-N(18)-C(7)	106.6(6)
C(24)-C(26)-Ru(2)	68.8(4)	C(6)-N(18)-Ru(1)	130.8(5)
C(25)-C(26)-Ru(2)	69.4(5)	C(7)-N(18)-Ru(1)	120.3(4)
C(27)-C(26)-Ru(2)	137.2(5)	C(6)-N(23)-C(8)	107.2(6)
C(26)-C(27)-C(28)	116.0(8)	C(6)-N(23)-C(9)	129.2(6)
C(26)-C(27)-C(29)	107.2(7)	C(8)-N(23)-C(9)	123.3(6)
C(28)-C(27)-C(29)	109.6(8)	C(2)-N(24)-C(4)	108.1(6)
C(26)-C(27)-H(27)	107.9	C(2)-N(24)-C(5)	127.2(6)
C(28)-C(27)-H(27)	107.9	C(4)-N(24)-C(5)	124.4(6)
C(29)-C(27)-H(27)	107.9	C(2)-P(1)-C(6)	100.6(3)
C(27)-C(28)-H(28A)	109.5	C(2)-P(1)-C(1)	99.3(3)
C(27)-C(28)-H(28B)	109.5	C(6)-P(1)-C(1)	99.3(3)
H(28A)-C(28)-H(28B)	109.5	C(2)-P(1)-Ru(2)	118.3(2)
C(27)-C(28)-H(28C)	109.5	C(6)-P(1)-Ru(2)	117.1(2)
H(28A)-C(28)-H(28C)	109.5	C(1)-P(1)-Ru(2)	118.7(2)
H(28B)-C(28)-H(28C)	109.5		

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z+3/2

Table ESI2. Bond lengths [Å] and angles [°] for **5**·4CH_3OH.

Ru(1)-N(3)	2.0927(9)	C(9)-N(4)	1.4687(16)
Ru(1)-N(1)	2.1058(9)	C(9)-H(9A)	0.9800
Ru(1)-C(13)	2.1779(12)	C(9)-H(9B)	0.9800
Ru(1)-C(12)	2.1846(11)	C(9)-H(9C)	0.9800
Ru(1)-C(14)	2.1889(11)	C(10)-C(11)	1.5000(19)
Ru(1)-C(15)	2.2063(11)	C(10)-H(10C)	0.9800
Ru(1)-C(11)	2.2239(12)	C(10)-H(10B)	0.9800
Ru(1)-C(16)	2.2450(11)	C(10)-H(10A)	0.9800
Ru(1)-Cl(1)	2.3921(3)	C(11)-C(12)	1.4064(19)
C(1)-C(1)#1	1.530(2)	C(11)-C(13)	1.4280(18)
C(1)-P(1)	1.7884(11)	C(12)-C(14)	1.4300(19)
C(1)-H(1A)	0.9900	C(12)-H(12A)	0.9500
C(1)-H(1B)	0.9900	C(13)-C(15)	1.4121(17)
C(2)-N(1)	1.3359(13)	C(13)-H(13A)	0.9500
C(2)-N(2)	1.3583(13)	C(14)-C(16)	1.4087(17)
C(2)-P(1)	1.7944(10)	C(14)-H(14A)	0.9500
C(3)-C(4)	1.3617(17)	C(15)-C(16)	1.4294(16)
C(3)-N(1)	1.3718(14)	C(15)-H(15A)	0.9500
C(3)-H(3A)	0.9500	C(16)-C(17)	1.5145(18)
C(4)-N(2)	1.3672(15)	C(17)-C(19)	1.527(2)
C(4)-H(4A)	0.9500	C(17)-C(18)	1.547(2)
C(5)-N(2)	1.4630(15)	C(17)-H(17)	1.0000
C(5)-H(5C)	0.9800	C(18)-H(18A)	0.9800
C(5)-H(5B)	0.9800	C(18)-H(18B)	0.9800
C(5)-H(5A)	0.9800	C(18)-H(18C)	0.9800
C(6)-N(3)	1.3403(13)	C(19)-H(19A)	0.9800
C(6)-N(4)	1.3577(14)	C(19)-H(19C)	0.9800
C(6)-P(1)	1.8059(11)	C(19)-H(19B)	0.9800
C(7)-C(8)	1.3650(17)	C(31)-O(31)	1.302(5)
C(7)-N(3)	1.3727(14)	C(31)-O(31B)	1.419(6)
C(7)-H(7A)	0.9500	O(1)-P(1)	1.4795(9)
C(8)-N(4)	1.3656(16)	C(32)-O(32)	1.401(4)
C(8)-H(8A)	0.9500	C(32)-O(32B)	1.447(5)

N(3)-Ru(1)-N(1)	85.09(3)	C(1)#1-C(1)-H(1B)	109.7
N(3)-Ru(1)-C(13)	124.50(4)	P(1)-C(1)-H(1B)	109.7
N(1)-Ru(1)-C(13)	92.37(4)	H(1A)-C(1)-H(1B)	108.2
N(3)-Ru(1)-C(12)	152.91(4)	N(1)-C(2)-N(2)	109.98(9)
N(1)-Ru(1)-C(12)	120.42(4)	N(1)-C(2)-P(1)	124.51(7)
C(13)-Ru(1)-C(12)	67.57(5)	N(2)-C(2)-P(1)	125.27(8)
N(3)-Ru(1)-C(14)	115.74(4)	C(4)-C(3)-N(1)	109.08(10)
N(1)-Ru(1)-C(14)	158.52(4)	C(4)-C(3)-H(3A)	125.5
C(13)-Ru(1)-C(14)	80.30(5)	N(1)-C(3)-H(3A)	125.5
C(12)-Ru(1)-C(14)	38.17(5)	C(3)-C(4)-N(2)	106.86(10)
N(3)-Ru(1)-C(15)	97.08(4)	C(3)-C(4)-H(4A)	126.6
N(1)-Ru(1)-C(15)	117.75(4)	N(2)-C(4)-H(4A)	126.6
C(13)-Ru(1)-C(15)	37.57(5)	N(2)-C(5)-H(5C)	109.5
C(12)-Ru(1)-C(15)	79.68(5)	N(2)-C(5)-H(5B)	109.5
C(14)-Ru(1)-C(15)	67.23(4)	H(5C)-C(5)-H(5B)	109.5
N(3)-Ru(1)-C(11)	162.31(4)	N(2)-C(5)-H(5A)	109.5
N(1)-Ru(1)-C(11)	93.67(4)	H(5C)-C(5)-H(5A)	109.5
C(13)-Ru(1)-C(11)	37.84(5)	H(5B)-C(5)-H(5A)	109.5
C(12)-Ru(1)-C(11)	37.19(5)	N(3)-C(6)-N(4)	109.60(9)
C(14)-Ru(1)-C(11)	68.17(5)	N(3)-C(6)-P(1)	124.98(8)
C(15)-Ru(1)-C(11)	67.87(5)	N(4)-C(6)-P(1)	125.34(8)
N(3)-Ru(1)-C(16)	93.28(4)	C(8)-C(7)-N(3)	108.47(10)
N(1)-Ru(1)-C(16)	154.84(4)	C(8)-C(7)-H(7A)	125.8
C(13)-Ru(1)-C(16)	67.92(4)	N(3)-C(7)-H(7A)	125.8
C(12)-Ru(1)-C(16)	67.70(5)	C(7)-C(8)-N(4)	107.24(10)
C(14)-Ru(1)-C(16)	37.02(4)	C(7)-C(8)-H(8A)	126.4
C(15)-Ru(1)-C(16)	37.45(4)	N(4)-C(8)-H(8A)	126.4
C(11)-Ru(1)-C(16)	80.36(5)	N(4)-C(9)-H(9A)	109.5
N(3)-Ru(1)-Cl(1)	84.53(3)	N(4)-C(9)-H(9B)	109.5
N(1)-Ru(1)-Cl(1)	83.63(3)	H(9A)-C(9)-H(9B)	109.5
C(13)-Ru(1)-Cl(1)	150.37(3)	N(4)-C(9)-H(9C)	109.5
C(12)-Ru(1)-Cl(1)	89.19(4)	H(9A)-C(9)-H(9C)	109.5
C(14)-Ru(1)-Cl(1)	92.78(3)	H(9B)-C(9)-H(9C)	109.5
C(15)-Ru(1)-Cl(1)	158.61(3)	C(11)-C(10)-H(10C)	109.5
C(11)-Ru(1)-Cl(1)	112.92(4)	C(11)-C(10)-H(10B)	109.5
C(16)-Ru(1)-Cl(1)	121.27(3)	H(10C)-C(10)-H(10B)	109.5
C(1)#1-C(1)-P(1)	109.93(10)	C(11)-C(10)-H(10A)	109.5
C(1)#1-C(1)-H(1A)	109.7	H(10C)-C(10)-H(10A)	109.5
P(1)-C(1)-H(1A)	109.7	H(10B)-C(10)-H(10A)	109.5

C(12)-C(11)-C(13)	117.71(11)
C(12)-C(11)-C(10)	122.01(12)
C(13)-C(11)-C(10)	120.24(12)
C(12)-C(11)-Ru(1)	69.88(7)
C(13)-C(11)-Ru(1)	69.33(6)
C(10)-C(11)-Ru(1)	130.28(10)
C(11)-C(12)-C(14)	121.38(11)
C(11)-C(12)-Ru(1)	72.92(7)
C(14)-C(12)-Ru(1)	71.08(6)
C(11)-C(12)-H(12A)	119.3
C(14)-C(12)-H(12A)	119.3
Ru(1)-C(12)-H(12A)	129.1
C(15)-C(13)-C(11)	121.12(11)
C(15)-C(13)-Ru(1)	72.30(7)
C(11)-C(13)-Ru(1)	72.83(7)
C(15)-C(13)-H(13A)	119.4
C(11)-C(13)-H(13A)	119.4
Ru(1)-C(13)-H(13A)	127.6
C(16)-C(14)-C(12)	120.78(11)
C(16)-C(14)-Ru(1)	73.65(6)
C(12)-C(14)-Ru(1)	70.75(6)
C(16)-C(14)-H(14A)	119.6
C(12)-C(14)-H(14A)	119.6
Ru(1)-C(14)-H(14A)	128.2
C(13)-C(15)-C(16)	120.84(11)
C(13)-C(15)-Ru(1)	70.12(7)
C(16)-C(15)-Ru(1)	72.74(6)
C(13)-C(15)-H(15A)	119.6
C(16)-C(15)-H(15A)	119.6
Ru(1)-C(15)-H(15A)	130.2
C(14)-C(16)-C(15)	118.03(11)
C(14)-C(16)-C(17)	119.84(11)
C(15)-C(16)-C(17)	122.13(11)
C(14)-C(16)-Ru(1)	69.32(6)
C(15)-C(16)-Ru(1)	69.81(6)
C(17)-C(16)-Ru(1)	133.20(9)
C(16)-C(17)-C(19)	114.47(11)

C(16)-C(17)-C(18)	106.74(13)	C(2)-N(1)-Ru(1)	129.24(7)
C(16)-C(17)-C(18)	106.74(13)	C(3)-N(1)-Ru(1)	124.02(7)
C(19)-C(17)-C(18)	111.32(14)	C(2)-N(2)-C(4)	107.50(9)
C(16)-C(17)-H(17)	108.0	C(2)-N(2)-C(5)	126.84(9)
C(19)-C(17)-H(17)	108.0	C(4)-N(2)-C(5)	125.01(10)
C(18)-C(17)-H(17)	108.0	C(6)-N(3)-C(7)	107.04(9)
C(17)-C(18)-H(18A)	109.5	C(6)-N(3)-Ru(1)	129.09(7)
C(17)-C(18)-H(18B)	109.5	C(7)-N(3)-Ru(1)	123.85(7)
H(18A)-C(18)-H(18B)	109.5	C(6)-N(4)-C(8)	107.64(9)
C(17)-C(18)-H(18C)	109.5	C(6)-N(4)-C(9)	128.23(10)
H(18A)-C(18)-H(18C)	109.5	C(8)-N(4)-C(9)	124.12(10)
H(18B)-C(18)-H(18C)	109.5	O(32)-C(32)-O(32B)	110.4(3)
C(17)-C(19)-H(19A)	109.5	O(1)-P(1)-C(1)	113.07(5)
C(17)-C(19)-H(19C)	109.5	O(1)-P(1)-C(2)	114.59(5)
H(19A)-C(19)-H(19C)	109.5	C(1)-P(1)-C(2)	107.32(5)
C(17)-C(19)-H(19B)	109.5	O(1)-P(1)-C(6)	112.82(5)
H(19A)-C(19)-H(19B)	109.5	C(1)-P(1)-C(6)	106.49(5)
H(19C)-C(19)-H(19B)	109.5	C(2)-P(1)-C(6)	101.61(5)
O(31)-C(31)-O(31B)	70.5(3)		
C(2)-N(1)-C(3)	106.57(9)		

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+1